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ORIGINAL ARTICLE

Utility of drain fluid amylase measurement on the first postoperative day after distal pancreatectomy

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Abstract

Background: Early exclusion of a postoperative pancreatic fistula (POPF) may facilitate earlier drain removal in selected patients after distal pancreatectomy. The purpose of this study was to evaluate the role of first postoperative day drain fluid amylase (DFA1) measurement to predict POPF.

Methods: Patients in whom DFA1 was measured after distal pancreatectomy were identified from a prospectively maintained database over a five-year period. A cut-off value of DFA1 was derived using ROC analysis, which yielded sensitivity and negative predictive value of 100% for excluding POPF.

Results: DFA1 was available in 53 of 138 (38%) patients who underwent distal pancreatectomy. 19 of 53 patients (36%) developed a pancreatic fistula (Grade A – 15, Grade B – 3, Grade C – 1). Median DFA1 was significantly higher in those who developed a pancreatic fistula (5473; range 613–28,450) compared those without (802; range 57–2350). $p < 0.0001$. Using ROC analysis, a DFA1 less than 600 excluded pancreatic fistula with a sensitivity of 100% (AUROC of 0.91; SE = 0.04, $p < 0.001$).

Conclusion: First postoperative day drain fluid amylase measurement may have a role in excluding pancreatic fistula after distal pancreatectomy. Such patients may be suitable for earlier drain removal.

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Introduction

Over the past decade there has been progressive reduction in the mortality following pancreatic resection which has been due to improvements in perioperative care and centralisation of services.[1,2] Despite these advances, morbidity remains high and is predominately due to post-operative pancreatic fistula (POPF) which develops in 16–28% of[3] patients. This may lead to complications including intra-abdominal collections, sepsis and secondary haemorrhage and death.[4,5] In 2005 the International Society Group for Pancreatic Fistulas (ISGPF) provided a uniform way of grading and reporting POPF[6] which has greatly reduced discrepancies in defining POPF between institutions.

There is good evidence that peritoneal drains after major abdominal surgery are not only unnecessary but may also be harmful.[7] However, due to the potential consequences of a pancreatic fistula, the vast majority of surgeons insert a peri-anastomotic drain after major pancreatic resection. In a multi-centre randomised clinical trial, Van Buren *et al.* reported a significant increase in mortality after pancreaticoduodenectomy in patients without drains.[7] Selective early drain removal has been shown to significantly reduce the risk of infectious complications after pancreaticoduodenectomy,[9] and has been successfully incorporated into enhanced recovery pathways.[9] Several studies have confirmed that measurement of drain fluid amylase on the first postoperative day (DFA1) after pancreaticoduodenectomy can accurately stratify patients at risk of pancreatic fistula, and may identify low risk patients who are suitable for early drain removal.[10] In contrast, there is limited evidence that DFA1 has clinical utility after distal pancreatectomy. The aim of this study was to evaluate the utility of DFA1 in excluding POPF in patients undergoing distal pancreatectomy.

Materials and methods

Patients who underwent distal pancreatectomy were identified from a prospectively maintained database between January 2010 and March 2016. Electronic case records were reviewed and patients who had a DFA1 measured were selected for further study.

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Drain fluid amylase was measured at the discretion of the operating surgeon and was not considered standard practice in the institution. Data regarding patient demographics, surgical approach, postoperative complications and histology were collected. POPF was defined and classified according to the ISGPF scheme. Patients who underwent both laparoscopic and open procedures were included in the study. At termination of surgery, a left sided drain was placed adjacent to the pancreatic transection site. Patients entered an enhanced recovery program with early mobilisation and return to normal diet as tolerated with low molecular weight heparin administered until discharge. Drains were removed if pancreatic fistula was excluded by a drain fluid amylase content less than 300 iU on the third post-operative day. Patients with a confirmed pancreatic fistula were discharged home with a drain in situ if clinically well. These patients were reviewed in clinic at 1–2 week intervals and the drain subsequently removed when the fistula had healed. The primary end-point was diagnosis of POPF and secondary outcomes were complications.

Statistical methods

Initially, demographic and surgical factors were compared between those patients who did and did not develop POPF. Continuous variables were not normally distributed, and were therefore reported as medians and interquartile ranges (IQR), with Mann–Whitney tests used for comparisons between groups. Comparisons of discrete variables were performed using Fisher's exact tests. The predictive accuracy of DFA on day 1 was then assessed using ROC curves. Further measures of predictive accuracy were then calculated, based on a range of cut-off values for DFA1. A subgroup analysis was also performed, calculating the area under the ROC curve (AUROC) for DFA1 within a range of different patient subgroups, to assess whether the predictive accuracy varied across factors. All analyses were performed using IBM SPSS 22 (IBM Corp., Armonk, NY), with $p < 0.05$ deemed to be indicative of statistical significance throughout. Patients with missing data were excluded on a per analysis basis.

Results

One hundred and fifty-three patients underwent distal pancreatectomy during the study period. The study group consisted of 53 patients in whom DFA1 was available. The median age of the study group was 64 years and there were 26 males and 27 females. The pathological diagnoses were neuroendocrine tumour ($n = 17$), adenocarcinoma ($n = 15$), mucinous cystic neoplasm ($n = 5$) chronic pancreatitis ($n = 3$), intra-ductal papillary mucinous neoplasm ($n = 3$), pseudopapillary tumours ($n = 2$) and other ($n = 7$). 24 patients in the study group underwent laparoscopic resection and 29 patients had open surgery. Overall, POPF developed in 28 patients (53%), the vast majority of which were grade A (21 out of 28). 7 patients (13%) developed a clinically significant POPF (grade B – 6; grade C – 1). Table 1 compares a range of factors between those patients who developed POPF, and those that did not. This found no significant differences for any of the demographic or surgical factors considered, although there was a trend for higher fistula rates in laparoscopic surgery (67% vs. 39% in Open, $p = 0.058$). There was no difference in hospital stay between those patients who developed POPF and those without (median number of inpatient days 6 (IQR 5–8) vs. 6 (IQR 5–11), $p = 523$). One patient died on post-operative day 88 due to respiratory failure without evidence of POPF. As anticipated the number of complications was higher in those with POPF. Four patients developed intra-abdominal collections, two required percutaneous drainage with one patient requiring re-laparotomy. Six patients developed complications unrelated to POPF, with no difference between the groups (Table 2).

Median DFA1 was found to be significantly higher in patients who developed POPF (3468 vs. 442; $p < 0.001$). ROC analysis (Fig. 1) returned an AUROC of 0.91 (SE = 0.04, $p < 0.001$) for the prediction of POPF using DFA1. The ability of DFA1 to identify patients at risk of clinically significant POPF (grades B and C) was found to be non-significant (AUROC = 0.65, SE = 0.08, $p = 0.207$). The predictive accuracy of a range of different cut-offs of DFA1 was then assessed (Table 3). No patients (0/14) with a DFA1 $\leq$ 600 developed a POPF, compared to 28/39 patients (72%) with a DFA1 > 600, yielding a sensitivity and specificity of 100% and 56%, respectively.

Discussion

Distal pancreatectomy consists of resection of that portion of pancreas extending to the left of the midline and not including the duodenum and distal bile duct.[8] Current indications include malignant tumours, cystic neoplasms, pseudocysts, chronic pancreatitis and trauma. Due to advances in surgical technique and perioperative care, mortality after distal pancreatectomy is in the range 0.9–1.4%.[11,12,9] However, morbidity occurs in up to one third of patients undergoing distal pancreatectomy, with POPF the most frequent complication. The reported incidence of POPF is 2–64.9%[10–12] within high volume centres and if left untreated can result in leakage of pancreatic enzymes into the peritoneal cavity which is associated with major complications including intra-abdominal collections, post-pancreatectomy haemorrhage[8,13] and delayed gastric emptying.[14,15]

In this study we report that a DFA1 of less than 600 excluded POPF with 100% sensitivity.

With higher DFA values the sensitivities and predictive value of excluding a POPF diminished. The value of DFA1 did not correlate or predict the grade of fistula. In the current series we report no mortality but POPF occurred in 53% patients which is higher than many standard published series. Of this cohort 75% were Grade A fistulas which represent sub-clinical leakage of amylase rich fluid from the pancreas which had no effect on the clinical course of the patient. Possible explanation for this may be the introduction of laparoscopic resections to the series and the associated learning curve. It is likely that in a number of

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Table 1 Patient and surgical characteristics

	Overall ($N = 53$)	Fistula		p-Value
		No ($N = 25$)	Yes ($N = 28$)	
Age	64 (54–72)	69 (51–72)	64 (54–73)	0.798
Gender				0.275
Female	27	15 (56%)	12 (44%)	
Male	26	10 (38%)	16 (62%)	
Indication				0.373
Adenoca	15	9 (60%)	6 (40%)	
NET	17	6 (35%)	11 (65%)	
Other	21	10 (48%)	11 (52%)	
Type of operation				0.098
Lap	24	8 (33%)	16 (67%)	
Open	29	17 (59%)	12 (41%)	
Stump				0.400
Staple	24	9 (38%)	15 (63%)	
Suture	27	14 (52%)	13 (48%)	
DFA on day 1	1718 (559–3512)	422 (173–953)	3468 (1780–6513)	**<0.001**

Data reported as median (IQR), with p-values from Mann–Whitney test, or as N (%), with p-values from Fisher's exact tests, as applicable. Bold p-values are significant at $p < 0.05$.

publications there has been under-reporting of POPF particularly in the pre-ISGF era.

The risk factors for POPF correspond to both patient-related and technical-related factors. The specific patient-related factors include male gender,[16] high BMI,[17] decreased serum albumin and high American Society of Anaestesiologist grade[13] and diabetes.[18] The texture of the gland in particular a soft pancreas with fatty infiltration and other anatomical features including small pancreatic duct and thick pancreatic remnant have been shown in retrospective series as independent risk factors for developing POPF.[13,16,19,20] However, the surgeon's description of the pancreatic gland as soft or firm is subjective and often inconsistent.[21] The two main techniques for closure of the pancreatic stump are suture closure of the pancreatic duct or stapled closure of the parenchyma.[22,23] Since it was first described in 1979 it has gained popularity as a simple and effective method of parenchymal transection.[12] The European Distal Pancreatectomy Trial Group compared hand-sewn closure with a stapling device and did not observe any significant difference in the incidence of

Table 2 Post-operative complications

Complication	Total
POPF	28
Grade A	21
Grade B	6
Grade C	1
Intra-abdominal collection	2
Pneumonia	1
Other	5
Wound infection	2
Urinary tract infection	1
Acute kidney injury	1
Haematoma	1

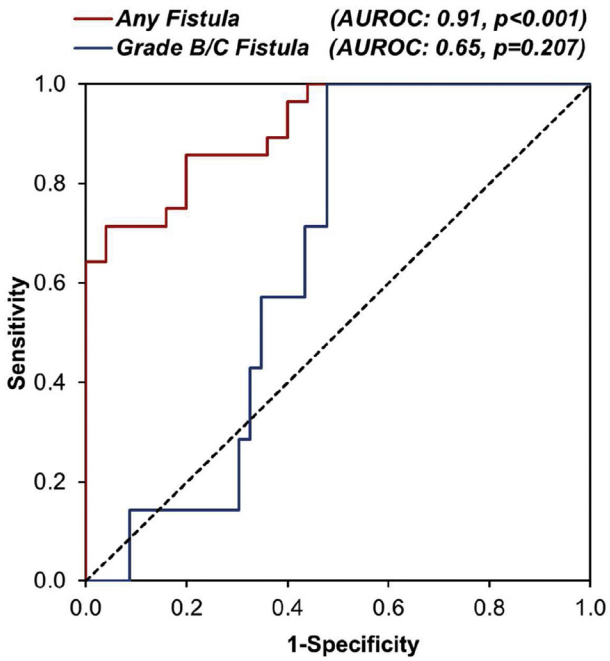

Figure 1 ROC curves for day 1 DFA

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Table 3 Predictive accuracy using different day 1 DFA cut-offs

Cut-off value	Fistula rate		Sensitivity	Specificity	PPV	NPV
	≤Cut-off value	>Cut-off value				
300	0/10 (0%)	28/43 (65%)	100%	40%	65%	100%
600	0/14 (0%)	28/39 (72%)	100%	56%	72%	100%
1000	4/24 (17%)	24/29 (83%)	86%	80%	83%	83%
2200	8/32 (25%)	20/21 (95%)	71%	96%	95%	75%

POPF.[23] Three meta-analyses on this topic have been performed. The first two did not show any difference between the two methods of closure[24,25] however the most recent review indicated that stapler was associated with a lower incidence of POPF compared with suture closure.[26] Several adjuncts have been described to reduced the incidence of leak at the transection site. Nakamura *et al.* described a technique of "prolonged peri-firing compression" with a linear stapler decreased the incidence of POPF.[27] This is believed to reduced trauma to the pancreatic ductules.[28] Other methods to reinforce the stump include coverage with autologous tissue,[29] fibrin glue[30,31] and fibrin sealant patch.[32] A recent Cochrane review failed to identify any evidence that fibrin sealants prevent POPF.[33]

The majority of POPF are managed conservatively with adequate drainage and antibiotics if there is evidence of systemic sepsis. Surgical drains were routinely placed at the end of the procedure. Typically located at the transection surface they can assist with detection of POPF and invariably provide adequate treatment in preventing complications by evacuating leaking pancreatic juices. Further radiological intervention for collections may be required if this provides inadequate drainage. In addition drains may also allow early identification of bleeding at the surgical bed.[34] There is abundant evidence in the literature from randomised clinical trials and meta-analysis that routine drainage after major gastrointestinal procedures increases infective complications particularly when left in place for prolonged periods of time.[35,36]

The evidence following pancreatic resection is less clear. In a non-randomised trial of 104 consecutive pancreatic head resections early drain removal on post-operative day 4 was shown to be an independent factor in reducing complications.[37] In a single centre randomised clinical trial, Conlon evaluated the role of routine intra-peritoneal drainage in 179 consecutive pancreaticoduodenectomies and found that omission of drains had no effect on morbidity or mortality.[38] The evidence that drainage after pancreas resection is harmful was challenged in a recent multi-centre randomised clinical trial involving 137 patients. Van Buren *et al.* reported a significantly increased mortality (3% vs. 12%) in the group without peritoneal drainage, resulting in early conclusion of the trial.[7] The concept of early and selective drain removal has been suggested as an effective compromise. In a randomised control trial Bassi *et al.* compared removal on day 3 vs. day 5 with decreased incidence of POPF with DFA1 < 5000 U/L.[39] Most series report primarily or exclusively on pancreaticoduodenectomy and there is a lack of data on drain management after distal pancreatectomy. In a retrospective review of 69 patients Paulus *et al.* reported morbidity in 49% of patients but did not observe a difference between the groups with no drainage.[34] In addition the presence of drains was infrequently helpful in identifying complications.

Early prediction of whether a patient is at low risk of POPF may help identify patients suitable for early drain removal. There is now growing evidence from a number of studies that measurement of a low DFA1 following pancreaticoduodenectomy can accurately exclude pancreatic fistula whilst being a simple and economic test.[40] Molinari *et al.* identified a cut off value of DFA1 of 5000 U/L predicted a POPF with a sensitivity and specificity of 93 and 84% and positive and predictive values of 59% and 98% respectively.[41] Sutcliffe *et al.* used a value of 350 U/L with a 100% sensitivity in developing pancreatic fistula.[2] In a recently published meta-analysis of drain amylase content on post-operative day 1 Gigilo *et al.* reported its accuracy in predicting POPF.[42] Cut off analysis of DFA <100, <350, <50,000 U/L had pooled sensitivities of 0.96, 0.91 and 0.59 with specificities of 0.5,0.84 and 0.91 respectively. The above studies were heterogenous as they included both pancreaticoduodenectomies and distal pancreatectomies in their analysis. As a consequence there is a lack of published data on DFA1 exclusive to distal resections. The first study to address this was Molinari *et al.*[41] who identified in 36 patients that a cut off DFA1 < 5000 had both a sensitivity and negative predictive value of 100% after distal pancreatectomy. In a large multi-centre retrospective review of patients undergoing pancreatic resection in the United States of America subgroup analysis of 180 distal pancreatectomies identified that DFA1 of <90 had a sensitivity and negative predictive value of 100%.[43] Overall pancreatic fistula occurred in 17.9% of patients. This group defined pancreatic fistula as "drainage of amylase rich fluid with drain continuation >7 days" and it is likely that there is under-reporting of subclinical Grade A fistulas. Recent work by Cirocchi *et al.*[44] reported that a DFA1 greater than 5000 was a predictive factor for pancreatic fistula in a retrospective series of 33 patients undergoing distal pancreatectomy.

The clinical role of DFA1 is that it can stratify patients who are at low risk of developing POPF and may be candidates for early drain removal and enhanced recovery after surgery (ERAS). Work in our institution demonstrated that a DFA1 < 350 after pancreaticoduodenectomy could successfully select patients for early diet and drain removal (POD3). This resulted in a reduced hospital in-patient stay and 30-day readmission rates. In this

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retrospective study we reported no POPF in patients with a DFA1 < 600 after distal pancreatectomy. Therefore, in this patient population prolonged intra-peritoneal drainage may offer no advantage and potentially increase complications. In contrast to pancreaticoduodenectomy, the role of routine prophylactic peritoneal drainage after distal pancreatectomy is less clear. In a retrospective study using propensity matching Behrman *et al.* demonstrated that prophylactic drainage of the surgical bed following distal pancreatectomy is associated with increased overall morbidity and pancreatic fistula.[45] Sub-group analysis indicated no difference in the incidence of serious morbidity and clinically relevant fistula. In a large series published by the Memorial Sloan Kettering group prophylactic drainage was omitted in nearly half of patients following distal pancreatectomy. No difference in the incidence of complications and need for percutaneous intervention.[46] Therefore there may be a role for 'selective' early drain removal in patients undergoing distal pancreatectomy and DFA1 may identify the patient population in whom its is appropriate for early drain removal.

This study has a number of limitations including its retrospective nature. DFA1 was not routinely measured in all patients and depended on surgical preference therefore a number of patients were excluded from this study. In addition, heterogeneity exists as both open and laparoscopic procedures were included in the study and methods of stump transection however the difference in POPF fistula did not reach statistical significance between the surgical approach. In conclusion, this retrospective study demonstrates that DFA1 can reliably exclude POPF in patients undergoing distal pancreatectomy. In patients with a DFA1 < 600 we suggest that it is safe to permit early drain removal and adhere to an enhanced recovery protocol.

Conflicts of interest

None declared.

References

1. Gooiker GA, van Gijn W, Wouters MW, Post PN, van de Velde CJ, Tollenaar RA *et al*. (2011) Systematic review and meta-analysis of the volume–outcome relationship in pancreatic surgery. *Br J Surg* 98: 485–494.
2. Sutcliffe RP, Battula N, Haque A, Ali A, Srinivasan P, Atkinson SW *et al*. (2012) Utility of drain fluid amylase measurement on the first postoperative day after pancreaticoduodenectomy. *World J Surg* 36: 879–883.
3. Kawai M, Tani M, Hirono S, Ina S, Miyazawa M, Yamaue H. (2009) How do we predict the clinically relevant pancreatic fistula after pancreaticoduodenectomy? – an analysis in 244 consecutive patients. *World J Surg* 33:2670–2678.
4. Butturini G, Daskalaki D, Molinari E, Scopelliti F, Casarotto A, Bassi C. (2008) Pancreatic fistula: definition and current problems. *J Hepatobiliary Pancreat Surg* 15:247–251.
5. Hackert T, Werner J, Buchler MW. (2011) Postoperative pancreatic fistula. *Surgeon* 9:211–217.
6. Bassi C, Dervenis C, Butturini G, Fingerhut A, Yeo C, Izbicki J *et al*. (2005) Postoperative pancreatic fistula: an international study group (ISGPF) definition. *Surgery* 138:8–13.
7. Van Buren, G, 2nd, Bloomston M, Hughes SJ, Winter J, Behrman SW, Zyromski NJ *et al*. (2014) A randomized prospective multicenter trial of pancreaticoduodenectomy with and without routine intraperitoneal drainage. *Ann Surg* 259:605–612.
8. Lillemoe KD, Kaushal S, Cameron JL, Sohn TA, Pitt HA, Yeo CJ. (1999) Distal pancreatectomy: indications and outcomes in 235 patients. *Ann Surg* 229:693–698. [Discussion 8–700].
9. Kollar D, Huszar T, Poharnok Z, Cselovszky E, Olah A. (2016) A review of techniques for closure of the pancreatic remnant following distal pancreatectomy. *Dig Surg* 33:320–328.
10. Fox AM, Pitzul K, Bhojani F, Kaplan M, Moulton CA, Wei AC *et al*. (2012) Comparison of outcomes and costs between laparoscopic distal pancreatectomy and open resection at a single center. *Surg Endosc* 26: 1220–1230.
11. Nakamura M, Wakabayashi G, Miyasaka Y, Tanaka M, Morikawa T, Unno M *et al*. (2015) Multicenter comparative study of laparoscopic and open distal pancreatectomy using propensity score-matching. *J Hepatobiliary Pancreat Sci* 22:731–736.
12. Miyasaka Y, Mori Y, Nakata K, Ohtsuka T, Nakamura M. (2017 Apr) Attempts to prevent postoperative pancreatic fistula after distal pancreatectomy. *Surg Today* 47:413–424.
13. Goh BK, Tan YM, Chung YF, Cheow PC, Ong HS, Chan WH *et al*. (2008) Critical appraisal of 232 consecutive distal pancreatectomies with emphasis on risk factors, outcome, and management of the postoperative pancreatic fistula: a 21-year experience at a single institution. *Arch Surg* 143:956–965.
14. Malleo G, Crippa S, Butturini G, Salvia R, Partelli S, Rossini R *et al*. (2010) Delayed gastric emptying after pylorus-preserving pancreaticoduodenectomy: validation of International Study Group of Pancreatic Surgery classification and analysis of risk factors. *HPB Oxf* 12:610–618.
15. Parmar AD, Sheffield KM, Vargas GM, Pitt HA, Kilbane EM, Hall BL *et al*. (2013) Factors associated with delayed gastric emptying after pancreaticoduodenectomy. *HPB Oxf* 15:763–772.
16. Ferrone CR, Warshaw AL, Rattner DW, Berger D, Zheng H, Rawal B *et al*. (2008) Pancreatic fistula rates after 462 distal pancreatectomies: staplers do not decrease fistula rates. *J Gastrointest Surg* 12: 1691–1697. [Discussion 7–8].
17. Hashimoto Y, Traverso LW. (2012) After distal pancreatectomy pancreatic leakage from the stump of the pancreas may be due to drain failure or pancreatic ductal back pressure. *J Gastrointest Surg* 16:993–1003.
18. Roberts KJ, Storey R, Hodson J, Smith AM, Morris-Stiff G. (2013) Preoperative prediction of pancreatic fistula: is it possible? *Pancreatology* 13:423–428.
19. Sledzianowski JF, Duffas JP, Muscari F, Suc B, Fourtanier F. (2005) Risk factors for mortality and intra-abdominal morbidity after distal pancreatectomy. *Surgery* 137:180–185.
20. Yang YM, Tian XD, Zhuang Y, Wang WM, Wan YL, Huang YT. (2005) Risk factors of pancreatic leakage after pancreaticoduodenectomy. *World J Gastroenterol* 11:2456–2461.
21. Jutric Z, Johnston WC, Grendar J, Haykin L, Mathews C, Harmon LK *et al*. (2016) Preoperative computed tomography scan to predict pancreatic fistula after distal pancreatectomy using gland and tumor characteristics. *Am J Surg* 211:871–876.

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22. Harris LJ, Abdollahi H, Newhook T, Sauter PK, Crawford AG, Chojnacki KA *et al*. (2010) Optimal technical management of stump closure following distal pancreatectomy: a retrospective review of 215 cases. *J Gastrointest Surg* 14:998–1005.
23. Diener MK, Seiler CM, Rossion I, Kleeff J, Glanemann M, Butturini G *et al*. (2011) Efficacy of stapler versus hand-sewn closure after distal pancreatectomy (DISPACT): a randomised, controlled multicentre trial. *Lancet* 377:1514–1522.
24. Knaebel HP, Diener MK, Wente MN, Buchler MW, Seiler CM. (2005) Systematic review and meta-analysis of technique for closure of the pancreatic remnant after distal pancreatectomy. *Br J Surg* 92:539–546.
25. Zhou W, Lv R, Wang X, Mou Y, Cai X, Herr I. (2010) Stapler vs suture closure of pancreatic remnant after distal pancreatectomy: a meta-analysis. *Am J Surg* 200:529–536.
26. Zhang H, Zhu F, Shen M, Tian R, Shi CJ, Wang X *et al*. (2015) Systematic review and meta-analysis comparing three techniques for pancreatic remnant closure following distal pancreatectomy. *Br J Surg* 102:4–15.
27. Nakamura M, Ueda J, Kohno H, Aly MY, Takahata S, Shimizu S *et al*. (2011) Prolonged peri-firing compression with a linear stapler prevents pancreatic fistula in laparoscopic distal pancreatectomy. *Surg Endosc* 25:867–871.
28. Misawa T, Shiba H, Usuba T, Nojiri T, Uwagawa T, Ishida Y *et al*. (2008) Safe and quick distal pancreatectomy using a staggered six-row stapler. *Am J Surg* 195:115–118.
29. Hassenpflug M, Hartwig W, Strobel O, Hinz U, Hackert T, Fritz S *et al*. (2012) Decrease in clinically relevant pancreatic fistula by coverage of the pancreatic remnant after distal pancreatectomy. *Surgery* 152: S164–S171.
30. Kram HB, Clark SR, Ocampo HP, Yamaguchi MA, Shoemaker WC. (1991) Fibrin glue sealing of pancreatic injuries, resections, and anastomoses. *Am J Surg* 161:479–481. [Discussion 82].
31. Lillemoe KD, Cameron JL, Kim MP, Campbell KA, Sauter PK, Coleman JA *et al*. (2004) Does fibrin glue sealant decrease the rate of pancreatic fistula after pancreaticoduodenectomy? Results of a prospective randomized trial. *J Gastrointest Surg* 8:766–772. [Discussion 72–74].
32. D'Andrea AA, Costantino V, Sperti C, Pedrazzoli S. (1994) Human fibrin sealant in pancreatic surgery: it is useful in preventing fistulas? A prospective randomized study. *Ital J Gastroenterol* 26:283–286.
33. Cheng Y, Ye M, Xiong X, Peng S, Wu HM, Cheng N *et al*. (2016) Fibrin sealants for the prevention of postoperative pancreatic fistula following pancreatic surgery. *Cochrane Database Syst Rev* 2:CD009621.
34. Paulus EM, Zarzaur BL, Behrman SW. (2012) Routine peritoneal drainage of the surgical bed after elective distal pancreatectomy: is it necessary? *Am J Surg* 204:422–427.
35. Monson JR, Guillou PJ, Keane FB, Tanner WA, Brennan TG. (1991) Cholecystectomy is safer without drainage: the results of a prospective, randomized clinical trial. *Surgery* 109:740–746.
36. Pai D, Sharma A, Kanungo R, Jagdish S, Gupta A. (1999) Role of abdominal drains in perforated duodenal ulcer patients: a prospective controlled study. *Aust N Z J Surg* 69:210–213.
37. Kawai M, Tani M, Terasawa H, Ina S, Hirono S, Nishioka R *et al*. (2006) Early removal of prophylactic drains reduces the risk of intra-abdominal infections in patients with pancreatic head resection: prospective study for 104 consecutive patients. *Ann Surg* 244:1–7.
38. Conlon KC, Labow D, Leung D, Smith A, Jarnagin W, Coit DG *et al*. (2001) Prospective randomized clinical trial of the value of intraperitoneal drainage after pancreatic resection. *Ann Surg* 234:487–493. [Discussion 93–94].
39. Bassi C, Molinari E, Malleo G, Crippa S, Butturini G, Salvia R *et al*. (2010) Early versus late drain removal after standard pancreatic resections: results of a prospective randomized trial. *Ann Surg* 252:207–214.
40. El Nakeeb A, Salah T, Sultan A, El Hemaly M, Askr W, Ezzat H *et al*. (2013) Pancreatic anastomotic leakage after pancreaticoduodenectomy. Risk factors, clinical predictors, and management (single center experience). *World J Surg* 37:1405–1418.
41. Molinari E, Bassi C, Salvia R, Butturini G, Crippa S, Talamini G *et al*. (2007) Amylase value in drains after pancreatic resection as predictive factor of postoperative pancreatic fistula: results of a prospective study in 137 patients. *Ann Surg* 246:281–287.
42. Giglio MC, Spalding DR, Giakoustidis A, Zarzavadjian Le Bian A, Jiao LR, Habib NA *et al*. (2016) Meta-analysis of drain amylase content on postoperative day 1 as a predictor of pancreatic fistula following pancreatic resection. *Br J Surg* 103:328–336.
43. Lee CW, Pitt HA, Riall TS, Ronnekleiv-Kelly SS, Israel JS, Leverson GE *et al*. (2014) Low drain fluid amylase predicts absence of pancreatic fistula following pancreatectomy. *J Gastrointest Surg* 18:1902–1910.
44. Cirocchi R, Graziosi L, Sanguinetti A, Boselli C, Polistena A, Renzi C *et al*. (2015) Can the measurement of amylase in drain after distal pancreatectomy predict post-operative pancreatic fistula? *Int J Surg* 21: S30–S33.
45. Behrman SW, Zarzaur BL, Parmar A, Riall TS, Hall BL, Pitt HA. (2015) Routine drainage of the operative bed following elective distal pancreatectomy does not reduce the occurrence of complications. *J Gastrointest Surg* 19:72–79. [Discussion 9].
46. Correa-Gallego C, Brennan MF, D'Angelica M, Fong Y, Dematteo RP, Kingham TP *et al*. (2013) Operative drainage following pancreatic resection: analysis of 1122 patients resected over 5 years at a single institution. *Ann Surg* 258:1051–1058.

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